Osteoporosis International (2019) 30:695–696
https://doi.org/10.1007/s00198-018-4785-1

LETTER TO THE EDITOR

Depression and antidepressant medications: both are linked to increased fracture risk

Q. Wu[1]

Received: 22 October 2018 / Accepted: 15 November 2018 / Published online: 28 November 2018

I thank Dr. Donzelli and his colleagues for their interest in our recent meta-analysis research. I agree that antidepressant use contributes to fracture risk and is associated with many other adverse effects. The scope of our meta-analysis was to investigate the association between depression, fracture risk, and bone loss [1]. Within that scope, we conducted a compressive meta-analysis and concluded that depression is associated with a significantly increased risk in fracture and bone loss. We also conducted subgroup analyses, and after controlling for antidepressant use found that the association between depression and fracture is significant. However, we did not "dismiss the possible additional contribution of antidepressant to fractures," or underestimate "antidepressants' role in risk of fractures." In fact, our prior meta-analyses, which focused on antidepressant use, demonstrated that either SSRIs [2] or TCA antidepressant [3] use is significantly associated with increased fracture risk.

Measuring the impact of depression on fracture risk remains a challenge when participants use antidepressants. Also, quantifying the influence of antidepressants on fracture risk is difficult when such an effect is confounded by indication or severity, factors which are concomitant with antidepressant medications. Our meta-analysis demonstrated depression is significantly associated with increased risk of fracture after adjusting for the effect of antidepressant use [1]. In addition, our prior meta-analyses showed that either SSRIs [2] or TCAs [3] exert an increased risk of fracture that is independent of depression. Although the underlying mechanisms of the impact of either depression or antidepressants on fracture risk have not been fully elucidated, the mechanisms are likely to be different: our meta-analyses indicated that declining BMD creates a pathway for depression that increases fracture risk [1, 4]; furthermore, one of our meta-analyses strongly suggested that the effect of TCAs increases the propensity for falling rather than causing bone loss [3]. Our additional meta-analysis also indicated that SSRIs may exert an increased risk of fracture independent of BMD reduction [2]. Depression can lead behavioral changes [5, 6] that might also affect BMD and fracture risk. Therefore, both depression and antidepressant medications are associated with increased risk of fracture; however, the underlying mechanisms are different.

I agree with Dr. Donzelli and his colleagues that "the promotion and prescription of physical activity and exercise, as well as effective psychotherapeutic interventions," are important to preventing and treating mild depression. On the other hand, clinical decision-making for individual patients should vary case by case. Clinicians should also be aware that different antidepressants have different adverse effects and different impacts on the risk of fracture due to variation in the basic mechanisms. Such impact also varies with the different duration of medications. For example, the increased risk of fracture with a shorter duration of TCA treatment (< 6 weeks) is much higher than that with extended treatment (≥ 6 weeks) [3]. Given this information, together with severity of depression, the effectiveness of non-medication treatments, should be considered together in clinic, in order to accurately determine if pharmacological therapies are needed and which medication(s) should be prescribed for individual patients.

Compliance with ethical standards

Disclosure summary The author has nothing to declare.

✉ Q. Wu
qing.wu@unlv.edu

[1] Department of Environmental & Occupational Health, School of Community Health Sciences, Nevada Institute of Personalized Medicine, University of Nevada, Las Vegas, NV 89154, USA

References

1. Wu Q, Liu B, Tonmoy S (2018) Depression and risk of fracture and bone loss: an updated meta-analysis of prospective studies. Osteoporos Int 29:1303–1312
2. Wu Q, Bencaz AF, Hentz JG, Crowell MD (2012) Selective serotonin reuptake inhibitor treatment and risk of fractures: a meta-analysis of cohort and case-control studies. Osteoporos Int 23:365–375
3. Wu Q, Qu W, Crowell MD, Hentz JG, Frey KA (2013) Tricyclic antidepressant use and risk of fractures: a meta-analysis of cohort and case-control studies. J Bone Miner Res 28:753–763
4. Wu Q, Liu J, Gallegos-Orozco JF, Hentz JG (2010) Depression, fracture risk, and bone loss: a meta-analysis of cohort studies. Osteoporos Int 21:1627–1635
5. Anda RF, Williamson DF, Escobedo LG, Mast EE, Giovino GA, Remington PL (1990) Depression and the dynamics of smoking. A national perspective. JAMA 264:1541–1545
6. Grant BF, Harford TC (1995) Comorbidity between DSM-IV alcohol use disorders and major depression: results of a national survey. Drug Alcohol Depend 39:197–206